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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/029,750      | 12/21/2001  | Ronghui Lin          | ORT-1554            | 4779             |

27777 7590 04/16/2004  
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NEW BRUNSWICK, NJ 08933-7003

EXAMINER

SHIAO, REI TSANG

ART UNIT PAPER NUMBER

1626

DATE MAILED: 04/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/029,750             | LIN ET AL.          |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Robert Shiao           | 1626                |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on responses filed on 2/23, 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-47 is/are pending in the application.
- 4a) Of the above claim(s) 24-35 and 45-47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-23 and 36-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
     a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                     | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                            | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>0404</u> . | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

1. This application claims benefit of the provisional application: 60/257,703 with a filing date 12/22, 2000.
2. Claims 1-47 are pending in the application.

### ***Responses to Election/Restriction***

3. Applicant's election without traverse of Group I claims 1-23, and 36-44, in part, in Paper No. 0204, dated February 23, 2004, is acknowledged. Claims 1-23, and 36-44, in part, are prosecuted in the case. Claims 1-23, and 36-44, in part (i.e., not embraced in Group I), 24-35, and 45-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

### ***Status of Claims***

4. Applicants elected Group I claims 1-23, and 36-44, in part, wherein the compound of formula (I) having 1,2,4-triazole moiety thereof. The scope of the invention of the elected subject matter is as follows:

A compound/composition of formula (I), wherein variables R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, and X are as defined in claim 1, except R<sub>1</sub> or R<sub>2</sub> does not represent heterocyclyl or heteroaryl; and wherein heterocyclyl and heteroaryl of R<sub>3</sub> or R<sub>4</sub> independently represents thienyl or imidazolynyl, or R<sub>3</sub> or R<sub>4</sub> independently represents triazole. The instant compounds are found in the pages 5-37 of the instant specification.

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The invention claims 1-23, and 36-44, in part, embraced in above elected subject matter are prosecuted in the case. Claims 1-23, and 36-44, in part, not embraced in above elected subject matter, and claims 24-35, and 45-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

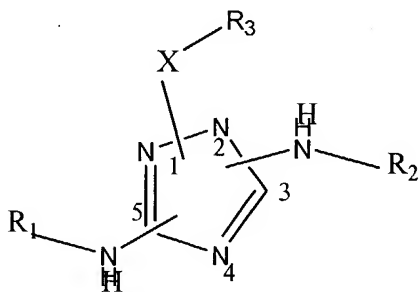
### ***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-23, and 36-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akahoshi et al. 5,750,545 and Kobayashi et al. publication, Yakugaku Zasshi, 1977, 97(9): 1039-45, see CAS:88:44882, in view of Okada et al. 5,674,886.

Applicants claim 1,2,4-triazole compounds/compositions of formula (I) as agents treating cancer,



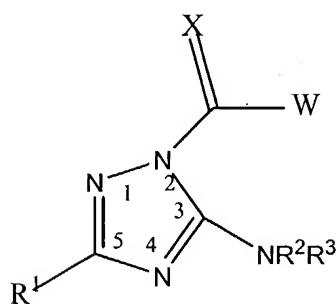
wherein the variable X represents -C(O), -C(S) and is linked to the 2<sup>nd</sup> position of the triazole ring; the variable R<sub>1</sub> represents C<sub>1-8</sub> alkyl, or aryl optionally substituted

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with alkyl or alkoxy, and the moiety  $R_1$ -NH- is linked to the 5<sup>th</sup> position of the triazole ring; the variable  $R_2$  represents hydrogen,  $C_{1-8}$  alkyl, and the moiety  $-NHR_2$  is linked to the 3<sup>rd</sup> position of the triazole ring; the variable  $R_3$  represents amino substituted with two substituents independently selected from the group consisting of hydrogen,  $C_{1-8}$  alkyl, and  $-C(O) C_{1-8}$  alkyl, and wherein heterocyclyl and heteroaryl of  $R_3$  or  $R_4$  independently represents thienyl or imidazolyl, or  $R_3$  or  $R_4$  independently represents triazole, and the moiety  $-XR_3$  is linked to the 2<sup>nd</sup> position of the triazole ring. The instant compounds are found in the pages 5-37 of the instant specification.

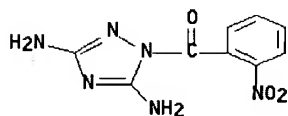
**Determination of the scope and content of the prior art (MPEP §2141.01)**

Akahoshi et al. disclose 1,2,4-triazole compounds of formula (I)



, wherein the variable X represents oxygen or sulfur atom, the variable W represents  $-NR^4R^5$ , and  $R^4$  and  $R^5$  independently represent hydrogen or lower alkyl; the variables  $R^2$  and  $R^3$  independently represent hydrogen or lower alkyl; the variable  $R^1$  represents  $-NR^{10}R^{11}$ , and variables  $R^{10}$  and  $R^{11}$  independently represent hydrogen, or phenyl optionally substituted with lower alkyl or lower alkoxy, see columns 2-7. A number of compounds have been specially exemplified in columns 14-55.

Kobayashi et al. disclose a compound 1H-1,2,4-Triazole-3,5-diamine, 1-(2-nitrobenzoyl)-,



**Determination of the difference between the prior art and the claims (MPEP §2141.02)**

The difference between the instant claims and Akahoshi et al. is that the variable R<sub>1</sub> of instant compounds represent C<sub>1-8</sub> alkyl, while Akahoshi et al. or Kobayashi et al. represent hydrogen at the same position.

Okada et al. disclose that 1,2,4-triazole compounds are agents of treating cancer, see abstract and columns 1-3, column 7, lines 32-66.

**Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)**

One having ordinary skill in the art would find the instant claims prima facie obvious **because** one would be motivated to employ the compounds of Akahoshi et al. and Kobayashi et al, and Okada et al. teachings to obtain a compound of formula (I), wherein the variable X represents –C(O), -C(S); the variable R<sub>1</sub> represents **methyl**, or aryl (i.e., phenyl) optionally substituted with alkyl, alkoxy; the variable R<sub>2</sub> represents hydrogen or **methyl**; the variable R<sub>3</sub> represents amino substituted with two substituents independently selected from the group consisting of hydrogen, C<sub>1-8</sub> alkyl, and –C(O) C<sub>1-8</sub> alkyl, or the variable R<sub>3</sub> represents aryl (i.e., phenyl) substituted with nitro.

It is well established that the substitution of methyl for hydrogen on a known compounds, i.e., replacement of the hydrogen (i.e., only one hydrogen) of variables  $R^2$ ,  $R^3$ ,  $R^{10}$ , and  $R^{11}$  of Akahoshi et al. with methyl, or replacement of the hydrogen (i.e., only one hydrogen) of  $-NH_2$  moiety of Okada et al. with methyl, is not a patentable modification absent unexpected or unobvious results, see *In re Wood*, 199 U.S.P.Q. 137 (C.C.P.A. 1978).

The motivation to make the claimed compounds derives from the expectation that the instant claimed compounds derived from known Akahoshi et al. and Kobayashi et al. compounds would possess similar activity (i.e., treating cancer) to that which is claimed in the reference.

### ***Objection***

6. Claims 1-23 (i.e., claim 1, line 19) are objected. Since the symbols (i.e., “), “(”, “{”, and “}”) are used in the claims, therefore, It is unclear the scope of  $-SO_2-$  or cycloalkyl of variable  $R_1$  in the claims. Replacement of the symbols with punctuations, i.e., “,” or “;”, would obviate the objection.

7. Claims 1-23, and 36-44 are objected as containing a non-elected invention. Deletion of the non-elected inventions, i.e., heteroaryl and heterocycle, the non-elected invention compounds of claims 18,21, 36, 43, and 44, would obviate the objection.

8. Claims 1-23, and 36-44 are objected. Claim 1, i.e., page 3, line 25, recites the terms “hydroxy( $C_{1-8}$ )alkyl” and “hydroxy( $C_{1-8}$ )alkoxy, which seem to be the terms “-O( $C_{1-8}$ )alkyl” and “-O( $C_{1-8}$ )alkoxy”. Correction is required.

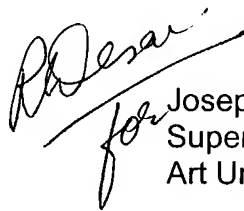
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***Telephone Inquiry***

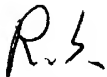
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in cursive script, appearing to read "J. McKane", with a horizontal line drawn through it.

Joseph K. McKane  
Supervisory Patent Examiner  
Art Unit 1626

A handwritten signature in cursive script, appearing to read "R. Shiao".

Robert Shiao, Ph.D.  
Patent Examiner  
Art Unit 1626

April 15, 2004